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The Correlation between the Body Mass Index and the Humoral Immune Response

العلاقة بين مؤشر كتلة الجسم والاستجابة المناعية الخلطية

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قسم علوم الحياة، كلية العلوم، جامعة الموصل، الموصل، العراق

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ABSTRACT

A limited number of studies have been carried out on the effect of obesity on the humoral immune system. Previous surveys showed that obesity in people and animals is associated with impaired immune function, specifically cell-mediated immunity. The aim of the current study is to compare the immunoglobulin concentrations among obese individuals in relation to their BMI and contrast them with normal values of non-obese individuals. This includes computing the correlation coefficient using a mathematical equation that measures the connection between immunoglobulins IgG, IgM and IgA, and BMI. To achieve these objectives, the study was carried out on 40 obese people (16 women and 24 men), aged between 20–45 years old, weighing between 85–129Kg and with heights between 154–188cm. All participants had a BMI between 35–44. The immunoglobulins values were obtained by using the radial immunodiffusion assay (Mancini method). The results showed a significant decrease in the levels of IgG, IgM, and IgA in obese individuals compared to non-obese individuals. Additionally, there was no correlation between BMI and IgG or IgM concentrations. Conversely, a correlation between BMI and IgA concentrations was observed. Moreover, the study succeeded in deriving a simple linear regression equation depending on the correlation coefficient. By using the SPSS 23 statistical analysis program, this equation allowed the researcher to calculate the concentration of IgA mathematically depending on the BMI value only. To the best of the researcher's knowledge. this research is considered the first of its kind in calculating IgA concentration depending on BMI value with no need to conduct the examination by using mathematical equation. The study concluded that obese people suffer from a deficiency in the humoral specific factors, which is probably reflected in the effectiveness of the humoral immune response to infectious agents and the appearance of autoantibodies in obese individuals when compared to non-obese individuals.

الملخص

عدد محدود من البحوث يدرس تأثير السمنة على الجهاز المناعي الخلطي. الدراسات السابقة اثبتت أن السمنة في النماذج البشرية الحيوانية تؤثر على الوظائف المناعية، وعلى وجه التحديد المناعة الخلوية. تتناول هذه الدراسة المناعة الخلطية عن طريق المقارنة بين مستويات الغلوبيولين المناعي بين الأفراد الذين يعانون من زيادة الوزن والسمنة مع القيم الطبيعية للأشخاص الذين لايعانون من السمنة، ومحاولة ايجاد معامل ارتباط بمعادلة رياضية يقيس العلاقة بين كل من الغلوبيولينات المناعية IgG وIgM وIgA، ومؤشر كتلة الجسم. وشملت الدراسة مشاركة 40 شخصا يعانون من السمنة المفرطة 16 نساء و 24 رجلاً تراوحت أعمارهم بين (20-45) سنة، والوزن (85-129 كجم) والطول (154-188 سم)، مع مؤشر لكتلة الجسم الذي تراوح بين(35-44)، تم الحصول على تراكيز الغلوبيولينات المناعية باستخدام طريقة مانسيني. اظهرت النتائج انخفاضًا كبيرًا في مستويات IgG و IgM و IgA لدى الأفراد البدينين مقارنة بالأفراد غير البدينين. كما أوضحت النتائج أنه لا يوجد معامل ارتباط بين مؤشر كتلة الجسم وتركيز كل IgG، IgM، وعلى العكس من ذلك، لوحظ وجود معامل ارتباط بين مؤشر كتلة الجسم وتركيز gA، واعتمادًا على هذا الارتباط، اوجدنا معادلة انحدار خطي بسيطة بواسطة برنامج التحليل الاحصائي SPSS وباستخدام هذه المعادلة، يمكننا تحديد تركيز IgA رياضيا اعتمادًا على قيمة مؤشر كتلة الجسم فقط. اضافة الى ذلك فأن هذه المعادلة تستنبط تركيز الغلوبيولين المناعي IgA في حالة زيادة او نقصان قيمة مؤشر كتلة الجسم، ويعد هذا البحث هو الاول من نوعه والذي يستخرج تركيز IgA دون الحاجة لإجراء الاختبار العملي لدى الأشخاص الأصحاء البدينين وغير البدينين. خلصت الدراسة الحالية إلى وجود خلل في العوامل الخلطية لدى الأشخاص الذين يعانون من السمنة، وهو ما ينعكس على فعالية الجهاز المناعي الخلطي لمقاومة عوامل الاصابة مما يشجع على الاجسام المضادة الذاتية في الفرد البدين مقارنة مع فرد غير البدين.

1. Introduction

Obesity is a remarkable burden on individual health, society, and the economy. Treatments for rising obesity and metabolic disorders are difficult tasks that involve efforts at every level of society. Obesity results from a high-energy diet that is characterised by an unusual or excessive accumulation of fat that can affect health (Schienkiewitz *et al.,* 2018:72). Obesity plays a critical role in cardiovascular, respiratory, renal, endocrine, and reproductive dysfunction, and contributes to severe metabolic disorders such as diabetes, liver disease, and atherosclerosis (Yosipovitch *et al.,* 2007:901; Schrijnders *et al.*, 2018:72). Obese individuals showed either elevated or reduced lymphocytes in peripheral blood (Andersen *et al.*, 2016:66; Green and Beck, 2017:S406), a reduced population of $CD8^+$T cells, and elevated or reduced population of $CD4^+$T cells (McLaughlin *et al.*, 2014:2637). They also displayed decreased proliferative lymphocyte reaction to activation by mitogens like Phytohaemagglutinin (PHA) and dysregulated cytokine activity. Both the number of NK cells and the cytotoxic activity in obese was people decreased (O'Shea *et al.*, 2010). Obesity was reported to be associated with a high level of leucocyte and lymphocytes excluding suppressor T cells, NK cells, reduced mutagenic proliferation of lymphocytes, increased monocyte, granulocyte, and phagocytosis process (Nielsen *et al.*, 1996:60).

In obese people, the risk of infection is greater than in non-obese people. In addition, inflammation caused by obesity is known to stimulate metabolic diseases. If there is imbalance between energy expenditure and energy intake, it can invoke both humoral and cell-mediated immune responses (Lumeng and Saltiel, 2011:2111). Obesity increases inflammatory cytokine formation, which further promotes inflammation of the body and may modify the immune system in human and animal design. (Samartin and Chandra, 2001:243). Immune cells, such as macrophages, microphages, and mast cells have been recorded to infiltrate adipose tissue (Gómez-Hernández *et al.*, 2016).

It is predicted that by 2030, the number of overweight adults all over the world (body mass index (BMI) > 25 kg/m^2) is expected to be 1.35 billion with 573 million of them considered clinically obese (BMI > 30 kg/m^2) (Kelly *et al.,* 2008:1431). BMI is a basic weight index based on height and is widely used for the classification of overweight and obese adolescents. It is described as a person's weight in kilograms split by a coefficient of their height in meters (kg/m^2) (Silver, 2015:1). Jih *et al.* (2014:1) stated the following ranges of body mass index (BMI) are used to describe levels of obesity: obese class I (moderate) is between 30–35, obese class II (severe obesity) is between 35–40, and obesity class III (very serious obesity) is above 40 kg/m^2. These classes are based on the World Health Organization (WHO) recommendations.

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In order to determine the effect of BMI on the concentration of some specific humoral compounds, this research estimated the levels of the main immunoglobulin IgG, IgM, IgA in obese people and compared them with the normal values of non-obese people. In addition, the research aimed to find the correlation coefficient of each immunoglobulin class IgG, IgM, IgA, and BMI.

2. Materials and Methods

The study was conducted on a group of obese students and teaching staff in the Biology Department, University of Mosul, Iraq for the period from 1/11/2018 to 1/5/2019. The participants included 40 obese people (16 women and 24 men), aged between 20–45 years, weighing between 85–129Kg, and with heights between 154–188cm. All participants had a BMI between 35–44.

2.1. Separation of Serum:

Five ml of whole blood was collected from each participant following standard procedures and using a serum separator tube (SST, tiger top tube). The samples were left to clot for one hour at room temperature and then centrifuged for ten minutes at approximately 1000 g. Using clean pipette technique, two ml of serum was aliquoted into labelled cryovials and immediately vials of serum were frozen at -80-degrees in a freezer.

2.2. Measurement of Immunoglobulin Concentration:

The immunoglobulin concentrations were extracted from the serum using the radial immunodiffusion assay (Mancini technique) and depended on the diameter of the ring of precipitation, which was associated with standardization values (see appendix) of each radial immunodiffusion plate batch from LTA Italian Company (Stites *et al.*, 1994).

2.3. Statistical Analysis:

Means were compared statistically using an Analysis of Variance (ANOVA) with probability P≤0.05. A correlation coefficient between BMI and IgG, IgM and IgA concentrations was found, and a simple linear regression equation was used to extract the IgA concentration depending on BMI only. Statistical analyses were conducted using SPSS 23 statistical analysis program .SPSS 23.0 software.

3. Results and Discussion

The results showed a significant decrease in IgG, IgM, and IgA in obese people compared to the control. The obtained results are shown in Tables (1), (2) and (3), respectively.

Table (1) The serum IgG concentration in obese people compared with the control

IgG mg/dl	Sample	Mean mg/dl ±SD	Extreme values mg/dl	P value
Obese	40	1046.0±228.33	574.6-1449.5	0.006*
Control	40	1294.1±305.49	809.3-1774.9	

*$P \leq 0.05$

Table (2) The serum IgM concentration in obese people compared with the control

IgM mg/dl	Sample	Mean mg/dl ±SD	Extreme values mg/dl	P value
Obese	40	101.25±44.02	51.5-167.5	0.0001*
Control	40	158.29±67.53	60.2-280	

*$P \leq 0.05$

Table (3) The serum IgA concentration in obese people compared with the control

IgA mg/dl	Sample	Mean mg/dl ±SD	Extreme values mg/dl	P value
Obese	40	147.84±46.233	68-232.3	0.0001*
Control	40	255.69±104.406	97.6-442.8	

*$P \leq 0.05$

The study showed a significant decrease in immunoglobulin levels in general. This study is inconsistent with the study conducted by (Mehta *et al.*, 2012: AB85), which showed insignificant differences in the concentrations of IgG and IgM but registered a significant increase in IgA concentration in obese children aged 7–15 years compared with the control. The study of Houjeghani *et al.* (2012:125) confirmed the effect of body mass on the immunoglobulin levels IgG, and IgA increased with high body mass. However, IgM levels showed low concentrations with high weight.

Another research indicated the reduced production of antibodies in obese people after vaccination relative to non-obese people (Martí *et al.*, 2001:138). Alternatively, the study done by Hruby and Hu (2015:673) suggested an insignificant effect of obesity on humoral immune response, especially the ones that are not associated with any health complications. Thus, the relationship between obesity and immunoglobulin levels in serum is not clearly understood and warrants further investigation.

To find the relationship between BMI and each concentration of the IgG, IgM, and IgA, the correlation coefficient was calculated. The results showed the lack of correlation coefficient between BMI and IgG or IgM, which was apparent in the weak inverse values (-0.267, -0.202) respectively shown in Table (4). On the other hand, the same test observed a strong, positive relationship between BMI and IgA (0.640) representing a strong difference (0.046) P≤0.05 as shown in Table (4).

Table (4) The correlation coefficient between BMI and IgG, IgM and IgA

		BMI	IgG	IgM	IgA
BMI	Pearson Correlation	1	-0.267-	-0.202-	0.640*
	Sig. (2-tailed)		0.456	0.576	0.046
	N	40	40	40	40
IgG	Pearson Correlation	-0.267-	1	0.742*	0.297
	Sig. (2-tailed)	0.456		0.014	0.404
	N	40	40	40	40
IgM	Pearson Correlation	0.202-	0.742*	-.1	0.320
	Sig. (2-tailed)	.576	.014		0.367
	N	40	40	40	40
IgA	Pearson Correlation	0.640*	0.297	0.320	1
	Sig. (2-tailed)	0.046	0.404	0.367	
	N	40	40	40	40

To measure the increase in the concentration of IgA in connection with the increase in BMI, a simple linear regression coefficient statistical test is shown in Figure (1). The estimations of concentration of IgA depending on BMI value only is also shown in Table (5).

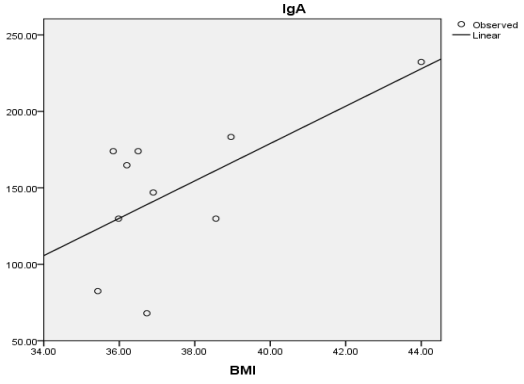
$$\mathrm{IgA} = \beta_o + \beta_1 BMI$$

IgA = -309.608 +12.215 *BMI

Table (5) Analysis of simple linear regression equation depending on BMI value

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant (β0)	β1
Linear	.409	5.541	1	8	.046	-309.608-	12.215

Fig(1) Simple linear equation depending on the correlation between BMI and IgA concentration



This is the first research of its kind where the researcher can estimate the concentration of immunoglobulin IgA based on the value of BMI and can use a simple linear regression equation in the statistical analysis program.

The findings of this study were in line with the study conducted by Al-Sufyani and Mahassni (2010:449). Their study showed a significant increase in the number of lymphocytes with no rise in B-cells in obese people compared to non-obese people. This means that the levels of IgA, IgM, and IgG free immunoglobulins should be within normal levels. However, the results of this study showed a significant decrease in the levels of free immunoglobulins, supporting the theory of an inflammatory process inside the body that leads to lower levels of free globulins to participate in controlling the inflammatory process.

The development of inflammatory status in obese people may explain the appearance of foreign antigens in fat tissue or blood vessels, which are required for the intervention of free immunoglobulins to control the inflammatory state in fat tissue. This hypothesis is confirmed by the study by Al-Sufyani and Mahassni (2010:449) who observed a significant rise in the number of neutrophil cells responsible for phagocytosis in obese individuals, which are higher when there is an inflammatory state inside the body. Trying to explain the immune changes in obese versus healthy people may seem extremely difficult because of multiple factors that affect and weaken the immune response, including increased leptin concentration. Leptin is an adiposity marker that has regulatory functions on specific and non-specific immunity (Marzullo *et al.*, 2014:398). In turn, it affects T cell effectiveness, as well as the appearance of autoantigens on the fatty tissue and the formation of immune complexes that stimulate B cells, producing autoantibodies and thus directing B cells from cells that work for the body into cells that produce autoantibodies. Leptin also serves as an IgA level predictor. (Marzullo *et al.*, 2014:398) research showed that IgM concentrations in obese patients were considerably reduced in combination with important increases in leukocyte counts. These are significantly associated with concentrations of leptin, lipid profile, insulin resistance, and adiposity. This situation and the important correlation between the concentrations of leptin and IgA may indicate an indirect leptin action in immunological changes resulting from obesity.

Nutritional status affects the immunological procedures engaged in the cooperative protection of humans. Consequently, a favourable chronic imbalance between energy intake and spending results in obesity cases, which may affect specific and non- specific immune responses. Also, a link between fatty tissue and immunocompetent cells has been supported by several lines of evidence. However, the comparison of immunity in obese and non-obese people, as well as the cellular and molecular processes involved, exists with restricted and often contentious data.

Generally, clinical and epidemiological data supports evidence that the incidence and severity of specific types of infectious diseases in obese people are higher than in non-obese people together due to weak antibody response in overweight individuals to antigens (Martí *et al.*, 2001).

The complexities and heterogeneity of the host defences regarding the immune response in various dietary conditions influencing the energy equilibrium involve an essential analysis of the immunocompetent cells. In this sense, further study is required to explain the clinical consequences of obesity-induced changes to immune function.

This study concluded that obese people suffer from a deficiency in the humoral specific factors, which is probably reflected in the effectiveness of the humoral immune response to infectious agents and the appearance of autoantibodies in obese individuals when compared to non-obese individuals.

Bio

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